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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/441,857	11/18/1999	HIAO-PENG XU DUFFY	52494/2202	5116

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EXAMINER

CANELLA, KAREN A

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/441,857

Applicant(s)

DUFFY ET AL.

Examiner

Karen A Canella

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 7-12, 70 and 81-91 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 83-91 is/are allowed.
- 6) ☒ Claim(s) 1, 7-12, 70, 81, 82 is/are rejected.
- 7) ☒ Claim(s) 2 and 3 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: ____.

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DETAILED ACTION

Claim 7-9 and 70 have been amended. Claims 81-89 have been added. Claims 1-3, 7-12, 70 and 81-89 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

The objection to claims 2 and 3, and claims 7-12 in part, for being dependent upon a rejected base claim, is maintained for reasons of record.

The rejection of claims 1, 7-12 and 70 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons of record. Newly added claims 81 and 82 are also rejected for the same reasons of record. Claim 1 is drawn to an isolated nucleic acid comprising a sequence encoding a wth3 protein. Claim 70 embodies the nucleic acid of claim 1 operatively linked to a regulatory sequence. Claims 7-12 are drawn in part to the nucleic acid of claim 1. Claim 81 is drawn to an isolated nucleic acid encoding a human wth3 protein. Claim 82 embodies the isolated nucleic acid of claim 81 wherein the wth3 protein is encoded from the chromosomal locus of 2q31.

The specification states on page 3, lines 15-18 that the isolate nucleic acids of the invention "can" encode an amino acid sequence comprising SEQ ID NO:12 from about amino acid residue number 1 to amino acid residue number 175 and that the nucleic acid sequence "can" be SEQ ID NO:7 or SEQ ID NO:11. Given the broadest reasonable interpretation, the nucleic acids of the invention are not confined to those encoding SEQ ID NO:12 and can include allelic variants, splice variants and nucleic acids encoding homologs and variant proteins differing in structure and function from SEQ ID NO:12.

The specification describes the nucleic acid sequences of SEQ ID NO:7 and 11 and the amino acid sequence of SEQ ID NO:12. The specification does not describe allelic variants or splice variants. The general knowledge of the art concerning allelic, polymorphic or splice

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variants does not provide any indication of how the structure of the polynucleotides encoding SEQ ID NO:12 are representative of the undisclosed allelic, polymorphic or splice variant sequences. The common attributes of this genus has not been described. With the exception of the nucleic acids encoding SEQ ID NO:12, one of skill in the art would conclude that the applicant was not in possession of the claimed genus because the species encoding SEQ ID NO:12 are not representative of all the variants of the genus and therefore insufficient to support the claim.

Further, the claims are broadly drawn to encompass nucleic acid encoding wth3 proteins beyond those limited to SEQ ID NO:12. The specification and claim 1 do not indicate what distinguishing attributes are shared by members of the genus of wth3 proteins. Thus, the specification does not place any limits on the number of amino acid substitutions, deletions, insertions or additions that may be made to SEQ ID NO:12 with the scope of a wth3 protein. Thus the scope of claim 1 is highly varied because a significant number of both structural and functional differences between members of the claimed genus is encompassed by the claim. Since the claim fails to limit the common attributes of the claimed genus in terms of both structure and function, and because the genus is highly variant, the polynucleotides encoding SEQ ID NO:12 are insufficient to describe the genus of polynucleotides encoding a wth3 protein. One of skill in the art would reasonably conclude that the specification fails to provide a representative number of species to describe the genus, and thus, the applicant was not in possession of the claimed genus at the time of filing.

Applicant has previously argued that the genus of wth3 proteins is well described by the specification specifically citing the location of the WTH3 protein in chromosome 2q31, the length of the mRNA transcript, the coding sequence and its homology to a family of proteins of known genetic function, and the downregulation of WTH3 in cells exhibiting multiple drug resistance and the differential methylation of WTH3. this has been considered but not found persuasive. The passages in the specification referred to in applicants argument do not represent a limiting definition for the genus of wth3 proteins, and exemplify only the instant disclosed WTH3 gene and protein translated therefrom. Even if the characteristics described by applicant were used as claim limitations, the claims would still read on a genus of proteins encompassing

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neutral allelic variants and homologs. The nature of both neutral allelic variants and homologs is that they are variant structures, and the structure of one does not serve to indicate the structure of other unknown allelic variants or homologs. The art teaches that an allele is an alternate form of a gene occupying the same locus in a particular chromosome and differing from other alleles at one or more mutational sites. The Glossary of Genetics (Reiger et al, 1991, pages 16-17) discloses that there are at least seven different kinds of allele in addition to the "strictly neutral" type. The alleles are distinguished by the effects that the different structural variant alleles have on phenotype, and thus different allelic proteins may function differently as a result of the alterations in amino acid sequence. There is no description in the specification of how the structure of SEQ ID NO:11 is related to the structure of other unknown alleles. With regard to homologs, it is known in the art that more often than not, a protein which is identified as a homolog in another species does not have the functional characteristics expected of said homolog based on the sequence homology between the two proteins. Bork and Koonin (Nature Genetics, 1998, Vol. 18, pp. 313-318) state that "more often than not, it is clear that the cellular role of the protein in question differs from that of the detected homologue(s) and there is currently no automatic means to establish how much functional information can be legitimately transferred by analogy from the homologue to the query (page 315, second column, lines 11-16, under the heading "Effects of noise on functional predictions"). Even in the event that the claims were amended to recite the limitations argued by the applicant, one of skill in the art would reasonable conclude that applicant did not disclose a representative number of species which would characterize the genus. Therefore, applicant was not in possession of the claimed genus.

Applicant argues in more detail that apart from the wth3 nucleic acids and proteins, the specification discloses the genetic locus of wth3 and that the genetic locus is a structural characteristic which defines wth3 and in particular describes variants such as allelic, polymorphic or splice variants. Applicant points out that the functional characteristic of the wth3 gene and protein in the enhancement of drug sensitivity. Applicant states that because of the disclosure of the structural and functional characteristics of the wth3 protein described therein, there is a correlation between function and structure for the claimed subject matter, this has been considered but not found persuasive. The description in the specification of the functional and structural properties of the human wth3 protein of SEQ ID NO:12 is not limiting

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for the instant claims which generically state “wth3” protein. For the reasons stated above, the specification clearly contemplates allelic sequences, and without a functional limitation recited in the claims, the claims encompass a genus of allelic sequences including sequences encoding variant proteins having different functional attributes from the instant SEQ ID NO:12.

Applicants arguments regarding the locus at which the wth3 protein is encoded from do not provide a structural or functional limitation for the nucleic acids encoding the wth3 protein because allelic variants as well as polymorphic and mutant sequences would also be encoded from the same locus.

Applicant argues that the findings of Bork and Koonin that functional predictions based on sequence homology do not apply to the instant invention, because the instant specification discloses actual functional characteristics of the wth3 protein. This has been considered but not found persuasive. Applicant has not provided the functional characteristics of the claimed homologues but has contemplated said homologues as part of the instant invention. Therefore, the functional attributes of any homologues would indeed be based on prediction, as no functional homologue has been disclosed by the specification. Further, without recitation of a functional limitation for the encoded proteins in the specification, the functional attributes of SEQ ID NO:12 as disclosed by the specification, would not be a limitation for the claimed subject matter.

All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicants amendments.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

6/14/2004


KAREN A. CANELLA PH.D
PRIMARY EXAMINER